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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,887	03/05/2002	Benjamin Eithan Reubinoff	13164A	7135

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Scully, Scott, Murphy & Presser
400 Garden City Plaza
Garden City, NY 11530

EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/090,887	REUBINOFF ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,34 and 36-45* is/are pending in the application.

4a) Of the above claim(s) *42-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33,34 and 36-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/436,164.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 17, 2005 has been entered.

DETAILED ACTION

This application filed March 5, 2002, is a divisional of 09/436,164, filed November 9, 1999, now US Patent 6,875,607, which claims benefit of foreign applications PP7009, filed November 9, 1998, and PQ2852, filed September 15, 1999, both filed in Australia.

Applicants' amendment filed June 17, 2005 has been received and entered. Claims 1-32 and 35 have been canceled. Claims 33 and 36-38 have been amended. Claims 39-45 have been added. Claims 33, 34 and 36-45 are pending and currently under examination.

Election/Restrictions

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Newly submitted claims 42-45 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 42-45 are directed to second different product. While the product can be used in the claimed methods, it can also be used for other cells or for other culturing conditions besides freezing of a cell or cell line.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 42-45 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Objections

Claims 37 and 38 objected to because the first presentation of an abbreviated term should be denoted by setting forth the full name indicating the term to be used subsequently, in particular the embodiments encompassing "hES" cell(s) is withdrawn.

The amendment to the claims has addressed the basis of the objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 36 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

The amendment to the claims to refer to methods recited in prior claims have addressed the basis of the rejection.

Claims 33 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. In this case, there are no active steps in the method claims only that the cells undergo vitrification, the omitted steps are ones that are drawn to the specific process of vitrification or more specifically to the OPS method.

Claims 36-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. With respect to the resulting cell, it is unclear how any form of cryopreservation would specifically affect the claimed cells. It does not appear that any method of cryopreservation results uniquely or completely in one affect, thus a cell frozen by one method may be the same as that frozen by another. The metes and bounds of the claim are vague and unclear as defined by "vitrified" because the same cryopreserved cell could also be found in other forms of preservation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Specifically, newly added claims recite vitrification buffers VS1 and VS2 comprising various specific components, however these are not supported and generally set forth in the claims. Upon review of the specification (paragraph 194) VS1 and VS2 are not specifically defined, however they are described in their use in the open pull straw vitrification method. Two points are at issue, first the specification only supports VS1 and VS with specific concentrations of the various listed components as well as those not recited but taught in the specification, and second, that VS1 and VS2 are only taught in the context of the open pull straw method.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 39-41 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. In this case, it is unclear that the breadth of any concentration of the listed components will be sufficient for use in the claimed methods.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the the time the application was filed...If a claim is

amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

Claim Rejections - 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 36-38 stand rejected under 35 U.S.C. 102(b) as being anticipate by Thomson *et al.* (Science 282:1145-1147-IDS Reference).

Applicants note the amendment to the claims to encompass cells that are "isolated" (claim 33) and which have been "vitrified" (claims 36-38) and argue that Thomson *et al.* fails to teach a vitrified hES cell or hES cell compositions. Applicants summarize the differences between different methods of cryopreservation (pages 4-7 and supporting references in Exhibit section) and argue that the disclosure of Thomson *et al.* of cryopreservation is insufficient to

anticipate a cell that has undergone vitrification as presently claimed (page 7). Applicants argue that the claimed composition can be distinguished from that disclosed by Thomson *et al.* See Applicants amendment, pages 4-8. Applicants' arguments have been fully considered, but not found persuasive.

Initially, it is noted that claim 38 encompasses undifferentiated and differentiated ES cells, and a reasonable interpretation of a product representing a differentiated ES cell would be any type of differentiated cell. Given this interpretation, any human cell type that was vitrified would anticipate the claims because of the embodiment of a "differentiated" cell. Turning to the rejection of record as anticipated by the teachings of Thomson *et al.*, Examiner would agree with Applicants that there are various methods of freezing cells, and each have inherent consequences in their practice. However, practicing one method, such as vitirification can also be practiced in a variety of ways with a variety of conditions, and even one method has a variety of inherent consequences. In this case, it is noted that the claims are broad and encompass practicing the method in a variety of different means or method steps. For example, though claim 39 lists specific components of a buffer that is contemplated for use, if one would use 90% DMSO versus 1%DMSO, clearly there would be a consequence on the end product. Finally, it is noted that in the breadth of the claims, there is no specific structural or functional requirement of the claimed hES cell or hES cell composition, only that it is cryopreserved by vitrification. The process of vitrification is one form of cryopreservation, and the result on the cell is simply that the cell is in a frozen state. What is being claimed is a hES cell line or hES cell composition, and without distinguishing functional or structural differences, a reasonable interpretation of the claims is a cryopreserved frozen hES cell, this accomplished by any methodology. As noted

previously, when the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "*prima facie* obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). In this case the claimed products can reasonably be interpreted to be a cryopreserved composition of human embryonic stem cells. Thomson *et al.* teaches that the cell lines disclosed in the reference were cryopreserved (second paragraph), and that after freezing the cell lines could be propagated without any apparent affect on the pluripotential characteristics of the cells.

Claims 36-38 stand rejected under 35 U.S.C. 102(e) as being anticipate by Thomson (US Patent 6,200,806-IDS Reference).

Applicants argue that similar to above for Thomson *et al.*, Thomosn fails to teach a vitrified hES cell or hES cell compositions. See Applicants amendment, page 8. Applicants' arguments have been fully considered, but not found persuasive.

As noted above in view of the breadth of the claims, there is no specific structural or functional requirement of the claimed hES cell or hES cell composition, only that it is cryopreserved by vitrification. While the process of vitrification is one form of

cryopreservation, and the result on the cell is simply that the cell is in a frozen state. What is being claimed is a hES cell line or hES cell composition, and without distinguishing functional or structural differences, a reasonable interpretation of the claims is a cryopreserved frozen hES cell, this accomplished by any methodology. As noted previously, when the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "*prima facie* obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). In this case the claimed products can reasonably be interpreted to be a cryopreserved composition of human embryonic stem cells. Thomson teaches that the cell lines disclosed in the reference were cryopreserved, and that after freezing the cell lines could be propagated without any apparent affect on the pluripotential characteristics of the cells (columns 14-15 and in Figure 6).

Claims 33 and 34 rejected under 35 U.S.C. 102(b) as being anticipate by Vajta *et al.* (Acta Vet Scan, 1997 or Mol Reprod Dev, 1998-IDS reference) is withdrawn.

Upon review of the teachings of Vajta *et al.* it is noted that porcine cells, not human cells are taught. Therefore, Vajta *et al.* fails to teach all the limitations of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomosn *et al.* (Science 282:1145-1147 or US Patent 6,200,806-IDS References) and Vajta *et al.*

Thomson teaches that the human embryonic cell lines disclosed in the reference were cryopreserved, and that after freezing the cell lines could be propagated without any apparent affect on the pluripotential characteristics of the cells (US Patent columns 14-15). At the time of filing cryopreserving a cell or cell line was routine in the art. Thomosn does not teach the specific method(s) of cryopreservation that are used, however it would be routine to use one known in the art that was successfully used to preserve other cell lines, in particular methods that were used for embryonic like cells. At the time of filing Vajta *et al.* teach that vitrification can be used for cryopreserving embryonic cells, and demonstrates the effectiveness by reducing to

practice the freezing of porcine embryos by the OPS method. The method set forth in claim 33 is broad and simply requires that the cell undergoes vitrification. Further, the cells of a developing embryo can be considered cells of a differentiated state (not totipoetent), and thus anticipate the embodiment of isolated differentiated human embryonic stem cells. The claims recite and encompass practicing the method with differentiated or undifferentiated cells, and the instant specification clearly teaches that the methodology contemplated is not new and refers to the methods taught by Vajta *et al.* (page 25, lines 2-4). While Vajta *et al.* teach that vitrification can be used for cryopreserving embryonic cells, ant that it can be extended to other mammals, they do not specifically teach that it should be practiced with human cells. Thomosn does not teach the specific method(s) of cryopreservation that are used, however it would be routine to use one known in the art that was successfully used to preserve other cell lines, in particular methods that were used for embryonic like cells.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the method of cryopreservation taught by Vajta *et al.* as one of the specific methods taught by Thomson for cryopreserving embryonic cells. One having ordinary skill in the art would have been motivated to use any specific method of cryopreservation known in the art, and there would have been a reasonable expectation of success given the results of Vajta *et al.* and the general disclosure of Thomson *et al.* to successfully cryopreserve a human embryonic stem cell.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claim is allowed.

As noted previously, the methods of cryopreserving a cell contemplated and used in the instant specification are not new and specfically refer to those disclosed by Vajta *et al.* Further, while Vajta *et al.* teaches generally that the method can be used in preserving undifferentiated embryonic cells (*i.e.* frozen embryos), Reubinoff *et al.* (Hum Reprod 16(10):2187-2194) teach that this method, the Open pulled Straw method for the vitrification of cells, can be successfully used in cryopreserving undifferentiated stem cells. Importanly, as suggested in the present specification, it is taught that the method does not result in any modification of the cells that are frozen, thus the methods of freezing would not provide a product that is distinguishable from that with which one started.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

Joe Woitach
AU1632